# Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV



Downloaded from https://aidsinfo.nih.gov/guidelines on 8/31/2020

**Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 1 of 3)

This table provides information on the known or predicted interactions between NRTIs and non-ARV drugs. Recommendations for managing a particular drug interaction may differ depending on whether a new ARV drug is being initiated in a patient on a stable concomitant medication or whether a new concomitant medication is being initiated in a patient on a stable ARV regimen. The magnitude and significance of drug interactions are difficult to predict when several drugs with competing metabolic pathways are prescribed concomitantly. In cases where an interacting drug needs to be replaced with an alternative, providers should exercise their clinical judgement to select the most appropriate alternative medication to use.

**Note:** Interactions associated with ddI and d4T are **not** included in this table. Please refer to the FDA product labels for ddI and d4T for information regarding drug interactions between these NRTIs and other drugs.

| Concomitant Drug | NRTI | Effect on NRTI and/or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **Cytomegalovirus and Hepatitis B Antivirals** | | | |
| Adefovir | TAF, TDF | No data | **Do not coadminister.** Serum concentrations of TDF and/or other renally eliminated drugs may increase. |
| **Ganciclovir, Valganciclovir** | TAF, TDF | No data | Serum concentrations of ganciclovir and/or TFV may increase. Monitor for dose-related toxicities. |
| | ZDV | ↔ ZDV expected<br>↔ ganciclovir expected | If coadministered, closely monitor for hematologic toxicities. |
| **Hepatitis C Antiviral Agents** | | | |
| **Glecaprevir/ Pibrentasvir** | TAF | ↔ TFV AUC | No dose adjustment needed. |
| | TDF | TFV AUC ↑ 29% | No dose adjustment needed. |
| **Ledipasvir/ Sofosbuvir** | TAF | TFV AUC ↑ 27% | No dose adjustment needed. |
| | TDF | Ledipasvir ↑ TFV AUC 40% to 98% when TDF is given with RPV and EFV<br>Ledipasvir ↑ TFV $C_{min}$ 55% to 80% when TDF is given with various PIs, NNRTIs, or INSTIs<br>Further ↑ TFV AUC and $C_{max}$ possible when TDF is given with PIs | **Do not coadminister** with EVG/c/TDF/FTC.<br>If TDF is used in these patients, monitor for TDF toxicities.<br>Consider using TAF in patients at risk of TDF-associated adverse events.<br>Consider using TAF or alternative HCV therapy in patients on TDF plus a PI/r or PI/c. The safety of increased TFV exposure with this combination has not been established. |
| **Ribavirin** | TDF | **Ribavirin With Sofosbuvir 400 mg:**<br>• ↔ TFV AUC | No dose adjustment needed. |
| | ZDV | Ribavirin inhibits phosphorylation of ZDV | Consider alternative. If coadministered, closely monitor HIV virologic response and monitor for possible hematologic toxicities. |
| **Sofosbuvir/ Velpatasvir** | TAF | ↔ TAF expected | No dose adjustment needed. |
| | TDF | TFV $C_{max}$ and AUC ↑ 39% to 81% when coadministered with various ARV combinations | If TDF is used in these patients, monitor for TDF-related toxicities.<br>Consider using TAF in patients at risk of TDF-related adverse events. |
| **Sofosbuvir/ Velpatasvir/ Voxilaprevir** | TAF | ↔ TAF expected | No dose adjustment needed. |
| | TDF | TFV $C_{max}$ and AUC ↑ 35% to 55% when coadministered with various ARV combinations | If TDF is used in these patients, monitor for TDF-related toxicities.<br>Consider using TAF in patients at risk of TDF-related adverse events. |

**Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 2 of 3)

| Concomitant Drug | NRTI | Effect on NRTI and/or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **INSTIs** | | | |
| **DTG** | TAF | ↔ TAF AUC | No dose adjustment needed. |
| | TDF | ↔ TDF AUC<br>↔ DTG AUC | No dose adjustment needed. |
| **RAL** | TDF | RAL AUC ↑ 49% | No dose adjustment needed. |
| **Narcotics and Treatment for Opioid Dependence** | | | |
| **Buprenorphine** | 3TC, TDF, ZDV | ↔ 3TC, TDF, ZDV, and buprenorphine | No dose adjustment needed. |
| | TAF | ↔ TAF expected | No dose adjustment needed. |
| **Methadone** | ABC | Methadone clearance ↑ 22% | No dose adjustment needed. |
| | ZDV | ZDV AUC ↑ 29% to 43% | Monitor for ZDV-related adverse effects. |
| **Other** | | | |
| **Anticonvulsants**<br>Carbamazepine, oxcarbazepine, phenobarbital, phenytoin | TAF | **With Carbamazepine:**<br>• TAF AUC ↓ 55%<br>↓ TAF possible with other anticonvulsants | **Do not coadminister.** |
| **Antimycobacterial**<br>Rifampin | TAF | **TAF with Rifampin Compared with TDF Alone:**<br>• TFV-DP AUC ↑ 4.2-fold<br>**TAF with Rifampin Compared with TAF Alone:**<br>• TAF AUC ↓ 55%<br>• TFV-DP AUC ↓ 36%<br>**TAF 25 mg Twice Daily with Rifampin Compared with TAF Once Daily Alone:**<br>• TAF AUC ↓ 14%<br>• TFV-DP AUC ↓ 24% | **Do not coadminister, unless benefits outweigh risks.**<br>Intracellular TFV-DP levels are higher when TAF is coadministered with rifampin compared to TDF administered alone, but clinical outcomes have not been studied. If coadministered, monitor virologic response. |
| | TDF | ↔ AUC TFV | No dose adjustment needed. |
| **Atovaquone** | ZDV | ZDV AUC ↑ 31% | Monitor for ZDV-related adverse effects. |
| **Rifabutin, Rifapentine** | TAF | ↓ TAF possible | **Do not coadminister.** |
| **St. John's Wort** | TAF | ↓ TAF possible | **Do not coadminister.** |
| **PIs for Treatment of HIV** | | | |
| **ATV (Unboosted), ATV/c, ATV/r** | TAF | **TAF 10 mg with ATV/r:**<br>• TAF AUC ↑ 91%<br>**TAF 10 mg with ATV/c:**<br>• TAF AUC ↑ 75% | No dose adjustment needed (use TAF 25 mg). |

**Table 21c. Drug Interactions Between Nucleoside Reverse Transcriptase Inhibitors and Other Drugs (Including Antiretroviral Agents) (Last updated December 18, 2019; last reviewed December 18, 2019)** (page 3 of 3)

| Concomitant Drug | NRTI | Effect on NRTI and/or Concomitant Drug Concentrations | Dosing Recommendations and Clinical Comments |
|---|---|---|---|
| **ATV (Unboosted), ATV/c, ATV/r** | TDF | **With ATV (Unboosted):**<br>• ATV AUC ↓ 25% and $C_{min}$ ↓ 23% to 40% (higher $C_{min}$ with RTV than without RTV)<br>TFV AUC ↑ 24% to 37% | **Do not coadminister unboosted ATV with TDF.**<br>Use ATV 300 mg daily plus (RTV 100 mg or COBI 150 mg) daily when coadministering TDF 300 mg daily.<br>If using TDF and an H2 receptor antagonist in an ART-experienced patient, use ATV 400 mg daily plus (RTV 100 mg or COBI 150 mg) daily.<br>Monitor for TDF-associated toxicities. |
| | ZDV | **With ATV (Unboosted):**<br>• ZDV $C_{min}$ ↓ 30% and ↔ ZDV AUC | Clinical significance unknown. If coadministered, monitor virologic response. |
| **DRV/c** | TAF | **TAF 25 mg with DRV/c:**<br>• ↔ TAF | No dose adjustment needed. |
| | TDF | ↑ TFV possible | Monitor for TDF-associated toxicities. |
| **DRV/r** | TAF | **TAF 10 mg with DRV/r:**<br>• ↔ TAF AUC | No dose adjustment needed. |
| | TDF | TFV AUC ↑ 22% and $C_{min}$ ↑ 37% | Clinical significance unknown. If coadministered, monitor for TDF-associated toxicities. |
| **LPV/r** | TAF | **TAF 10 mg with DRV/r:**<br>• TAF AUC ↑ 47% | No dose adjustment needed. |
| | TDF | ↔ LPV/r AUC<br>TFV AUC ↑ 32% | Clinical significance unknown. If coadministered, monitor for TDF-associated toxicities. |
| **TPV/r** | ABC | ABC AUC ↓ 35% to 44% | Clinical significance unknown. If coadministered, monitor virologic response. |
| | TAF | ↓ TAF expected | **Do not coadminister, unless benefits outweigh risks.** |
| | TDF | ↔ TDF AUC<br>TPV AUC ↓ 9% to 18% and $C_{min}$ ↓ 12% to 21% | No dose adjustment needed. |
| | ZDV | ZDV AUC ↓ 31% to 42%<br>↔ TPV AUC | Clinical significance unknown. If coadministered, monitor virologic response. |

**Key to Symbols:**

↑ = increase

↓ = decrease

↔ = no change

**Key:** 3TC = lamivudine; ABC = abacavir; ART = antiretroviral therapy; ARV = antiretroviral; ATV = atazanavir; ATV/c = atazanavir/cobicistat; ATV/r = atazanavir/ritonavir; AUC = area under the curve; $C_{min}$ = minimum plasma concentration; COBI = cobicistat; d4T = stavudine; ddI = didanosine; DRV/c = darunavir/cobicistat; DRV/r = darunavir/ritonavir; DTG = dolutegravir; EFV = efavirenz; EVG/c = elvitegravir/cobicistat; FDA = Food and Drug Administration; FTC = emtricitabine; HCV = hepatitis C virus; INSTI = integrase strand transfer inhibitor; LPV/r = lopinavir/ritonavir; NNRTI = non-nucleoside reverse transcriptase inhibitor; NRTI = nucleoside reverse transcriptase inhibitor; PI = protease inhibitor; PI/c = protease inhibitor/cobicistat; PI/r = protease inhibitor/ritonavir; RAL = raltegravir; RPV = rilpivirine; RTV = ritonavir; TAF = tenofovir alafenamide; TDF = tenofovir disoproxil fumarate; TFV = tenofovir; TFV-DP = tenofovir diphosphate; TPV/r = tipranavir/ritonavir; ZDV = zidovudine